



A Clear Vision For Life™

Ophthalmology Is Our Singular Focus



R&D Day 1

# Santen's Contribution to Ophthalmology

Global R&D

Santen Pharmaceutical Co., Ltd.

July 12<sup>th</sup>, 2019

# R&D Days



Day 1

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## Santen's Contribution to Ophthalmology

Introduction of Ophthalmology and Santen's Contribution  
Santen's Research and Development



Day 2

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## Santen's Future R&D

Long-term Perspective of Ophthalmology  
Santen's R&D approach

# Santen's Values and Mission Statement

Values

天機に参与する  
*Tenki ni sanyo suru*<sup>1</sup>

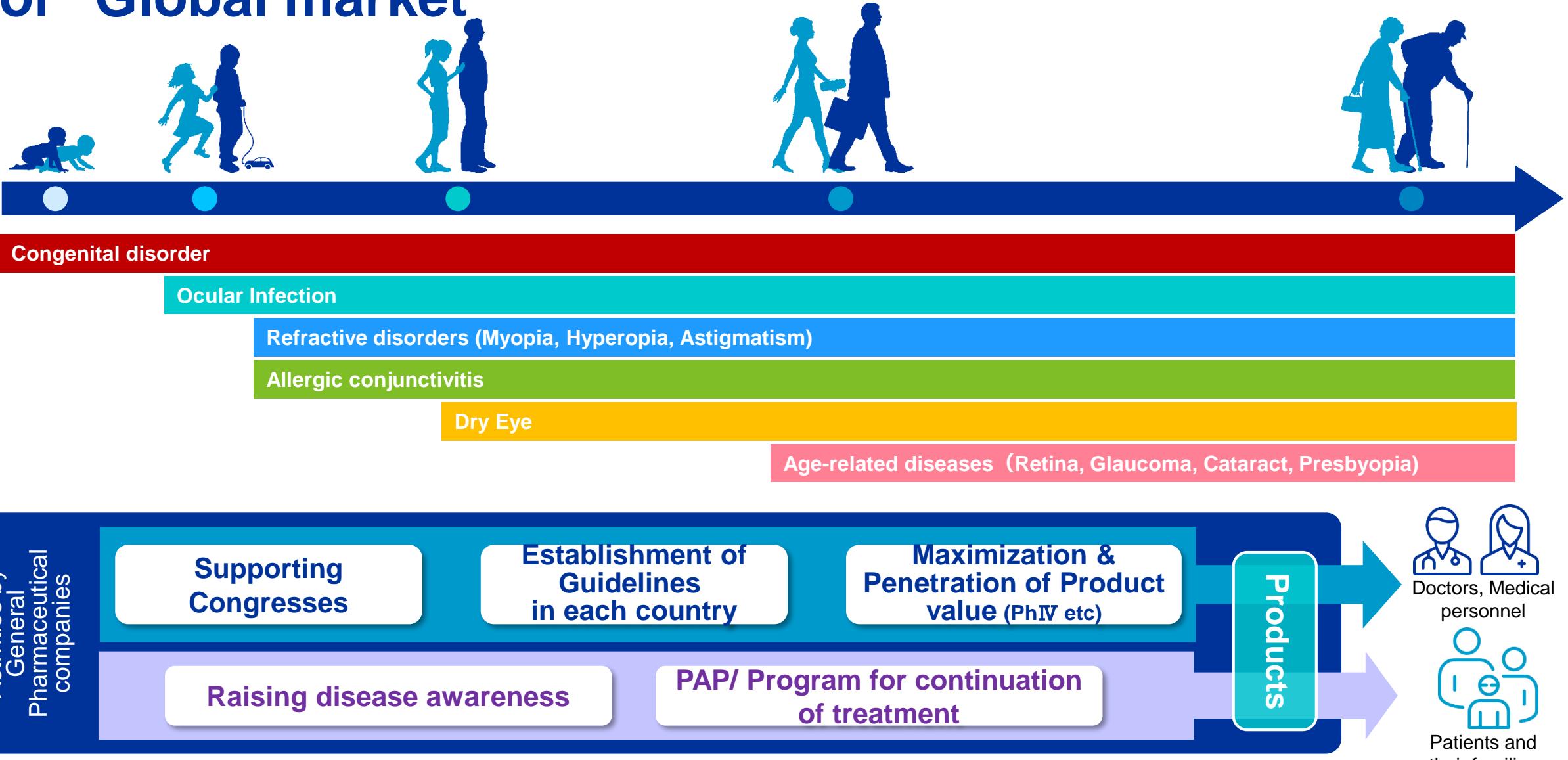
<sup>1</sup> “Exploring the secrets and mechanisms of nature in order to contribute to people’s health”  
Santen’s original interpretation of a passage from chapter 22 of *Zhongyong (The Doctrine of the Mean)* by Confucius.

**We think carefully about what is essential, decide clearly what we should do, and act quickly.**

Mission Statement

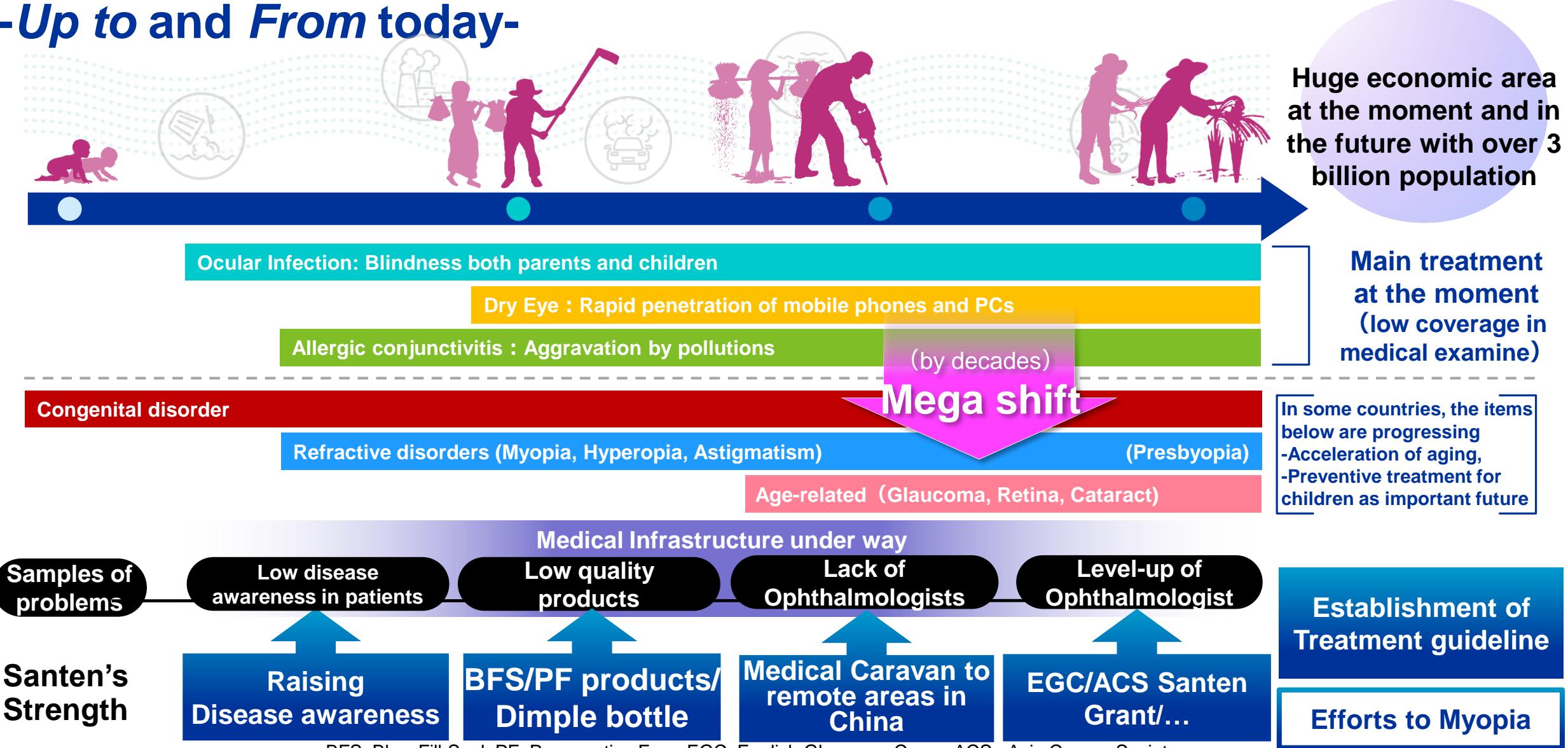
**By focusing on ophthalmology, Santen develops unique scientific knowledge and organizational capabilities that contribute to the well-being of patients, their loved ones and consequently to society.**

# Genericized "Life of Vision" in the framework of "Global market"



# Our original activities in Asia led Santen to No.1 in important markets

## -Up to and From today-



# Santen's business activities aiming to protect “Life of Vision” of people around the world

Affected

Diagnosis

Treatment initiation

Treatment period

Continuation of treatment

Global

Raising disease awareness

Improvement of diagnosis rate

Differentiated products

Improvement of compliance

Supports for stakeholders in ophthalmology

Stable supply

- Improvement of usability
- Minimally invasive

Advanced Countries

Prevention

New technology for diagnosis and treatment

Recurrence prevention

• Initiatives to age-related chronic disease

Developing Countries

Eco system

Raising and Supporting of ophthalmologists

Raising disease awareness

High quality products

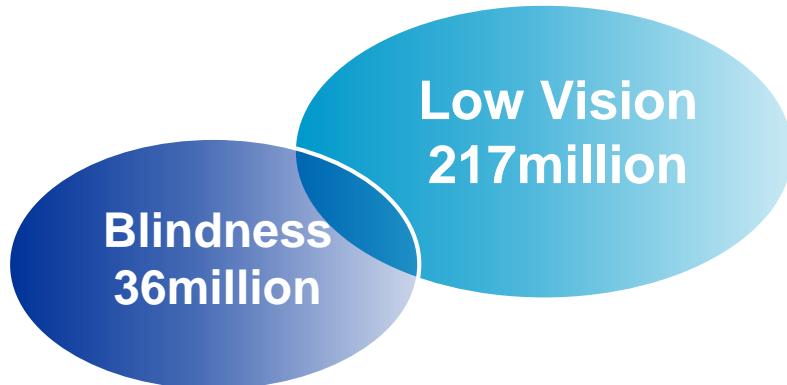
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# **Basic Policy on Santen R&D**

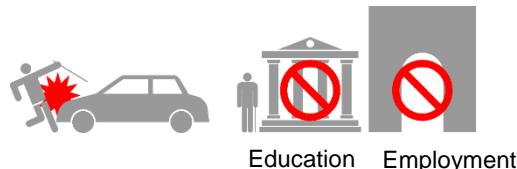
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# Protect the Sight of People Around the World

Ophthalmic market (2018)  
and number of patients



Vision impairment estimated  
impacting 1 in 30 of world  
population



Source: WHO World Sight Day Poster

## Cataract

Approx.  
**560M** patients

8B yen

## Glaucoma

Approx.  
**120M** patients

730B yen

## Dry Eye

Approx.  
**340M** patients

550B yen

## Myopia

Approx.  
**2600M** patients

Ocular  
Infection  
230B yen

Allergic  
Conjunctivitis  
200B yen

Anti-  
Inflammatory  
190B yen

**Retinal  
Diseases**

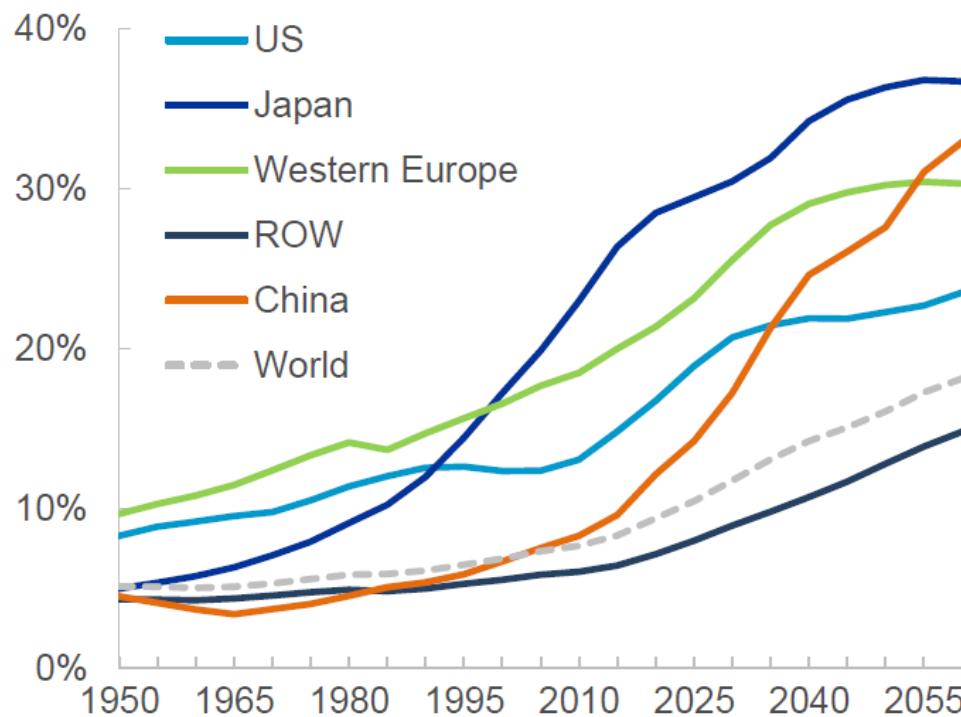
Approx.  
**270M** patients

860B yen

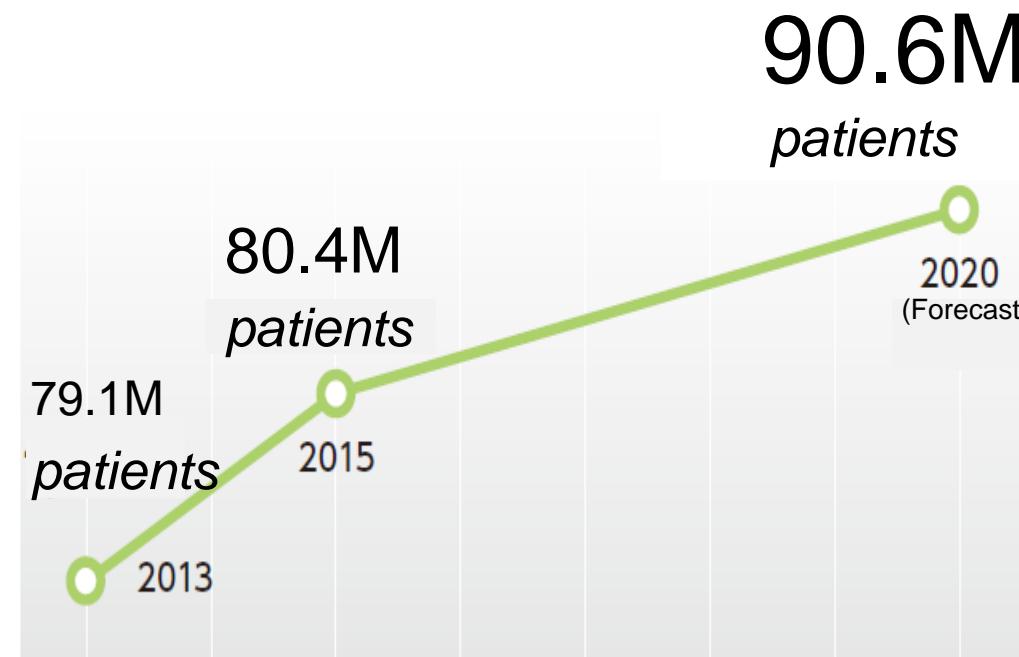
Source (Market): Copyright © 2019 IQVIA. IQVIA MIDAS 2018;  
Santen analysis based on IQVIA data. Reprinted with permission.

# Problem of Eye Disease Becoming Larger as the World Population is Aging

Population Aged 65+



Number of Glaucoma patients



Data Source: United Nations, World Population Prospects: 2015 Revision

Data Source: Market Scope; Santen analysis

# MTP2020 Fundamental Policy and Strategic Goals

## FUNDAMENTAL POLICY

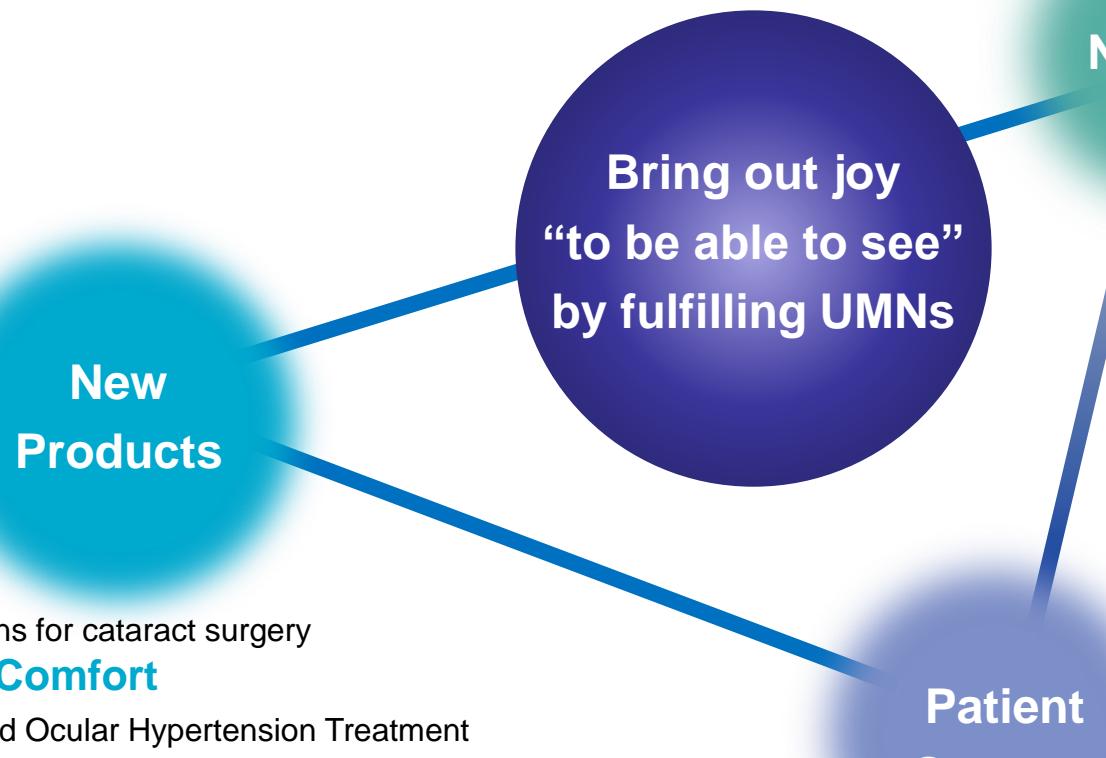
- To become a “Specialized Pharmaceutical Company with a Global Presence”
- Construct a path for sustainable growth beyond FY2020

## STRATEGIC GOALS



**Responding to the needs of patients and medical professionals worldwide,  
Santen will achieve reliable growth while sustainably contributing to  
ophthalmic treatment worldwide**

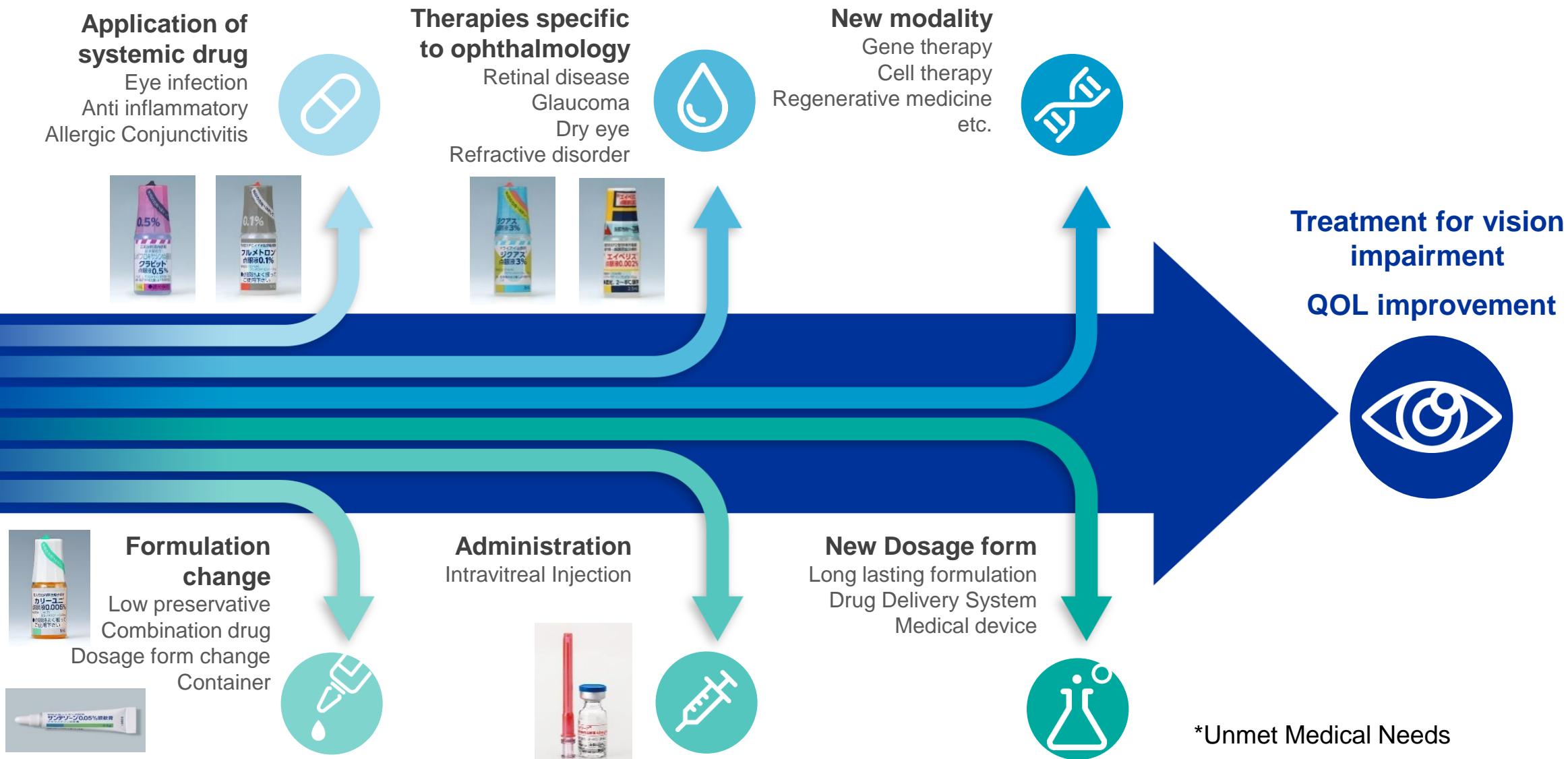
# Pursue development of much needed medical products, devices, information services by leveraging global R&D network



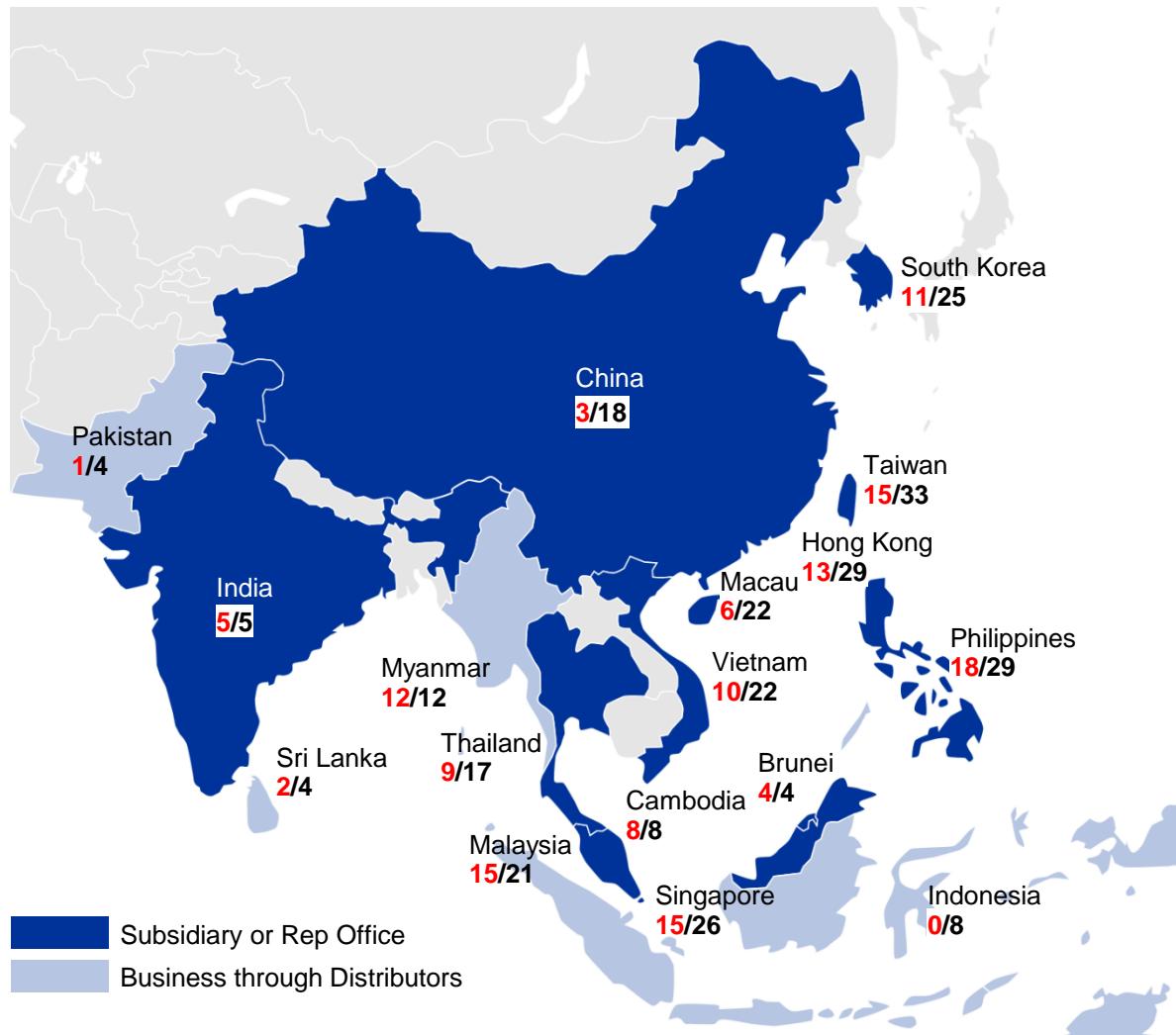
Aiming to provide treatment that will not be a burden to patients

Preservative free solution/container  
Assistive device for eye drop administration  
Improved distinguishability  
Drip prevention  
Easy to squeeze bottle

# Bring Out Joy “to be Able to See” by Fulfilling UMNs\*



# Proactively Introduce Products Approved in Japan & Europe to Asia



Registration Status in China



September 2015



October 2017

2015

2016

2017

Only 27 new products have been approved by China FDA



4,400 pharmaceutical companies, including 200 foreign companies

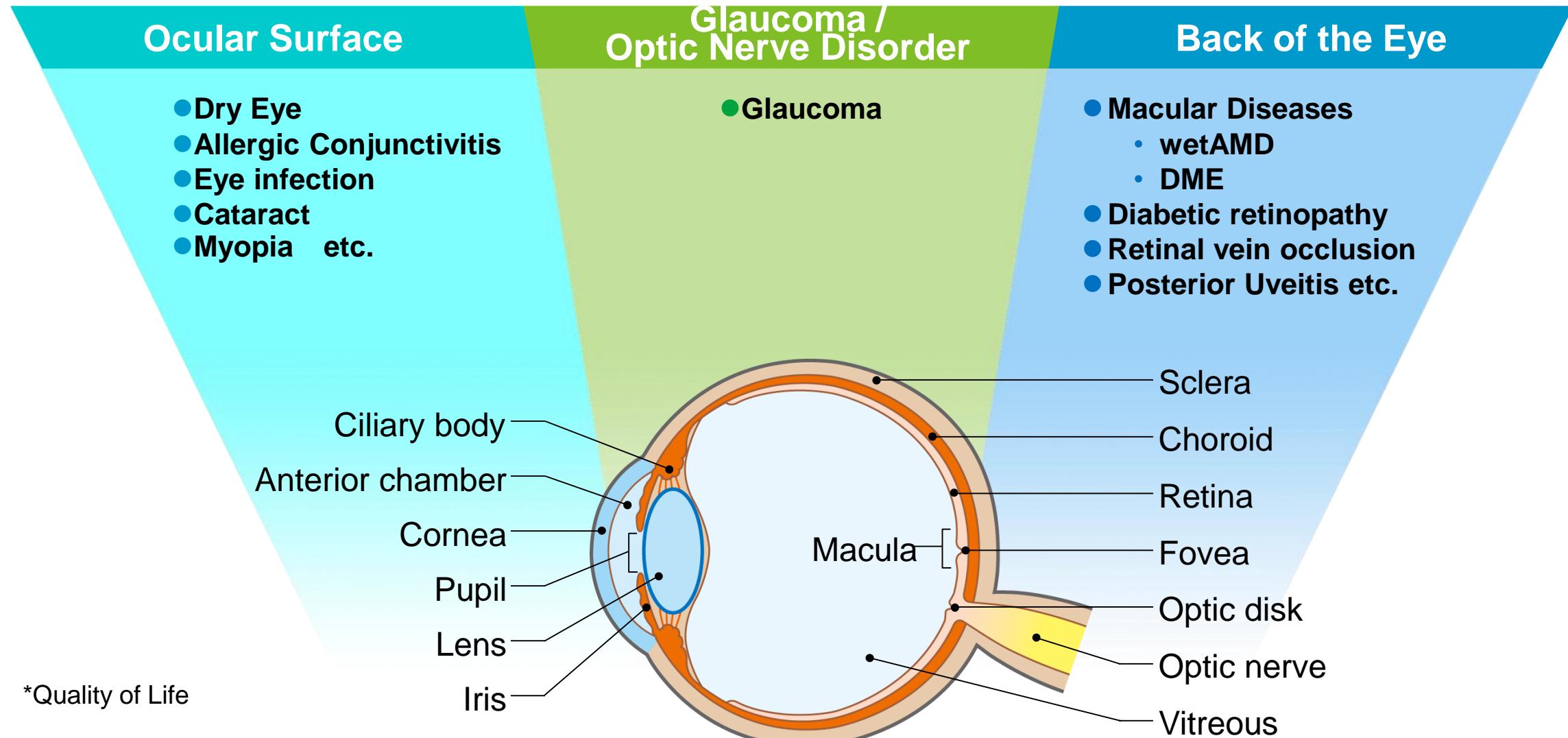
Only Santen for ophthalmic agent

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# Overview of Eye Diseases

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# Conducting R&D Specific to Ophthalmology to Contribute to Improving QOL\* in Patients Around the World

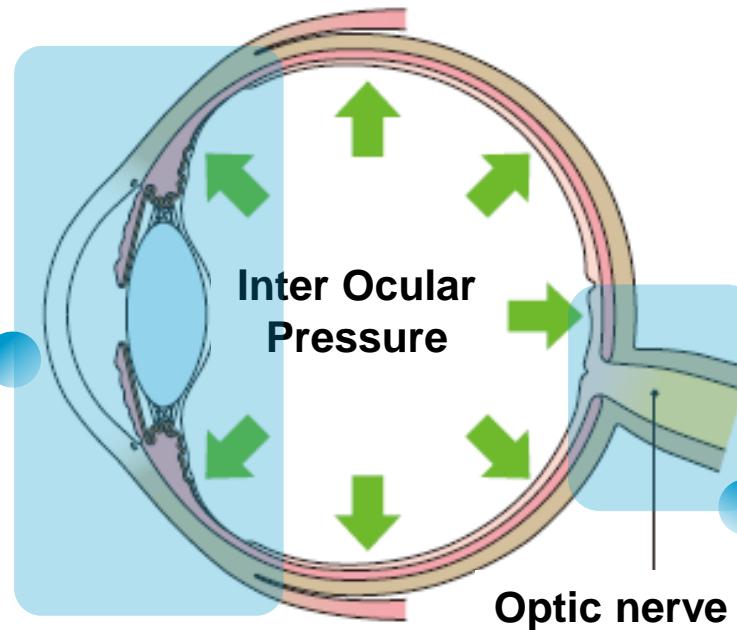


# Glaucoma: Preserve Visual Field by Lowering Intraocular Pressure

The No.2<sup>\*1</sup> cause of blindness in the world, No.1 in Japan<sup>\*2</sup>

Optic nerve damage  
due to high intraocular pressure

Inhibiting progressive  
visual field loss  
IOP lowering  
(Start/Continuation)



Visual field loss

Initial stage



Late stage



Image (Right eye only)

Keep and recovery of visual field

Neuroprotection

\*1: WHO Global Data on Visual Impairments 2010

\*2: Morizane et al, *Japanese Journal of Ophthalmology*, January 2019, Volume 63, 26–33

# Glaucoma: Respond to the Diverse Needs with Extensive Product Line



## ● IOP lowering agents (start)

Instillation to lower intraocular pressure



## ● IOP lowering agents (Continuation)

Continue treatment for a lifetime.  
Change or add the treatment depending on severity



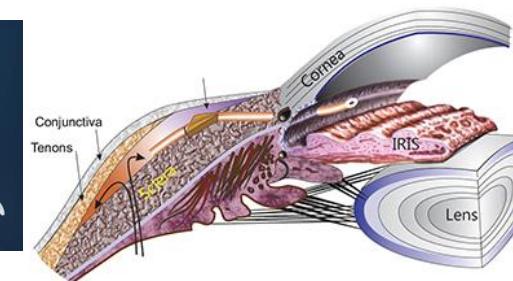
## ● Laser

The laser is applied to the part where the aqueous humor is discharged (trabecular meshwork) to promote the drainage.



## ● Surgery

Removes a part of trabecular meshwork and creates the drainage route for aqueous humor.  
e.g. Trabeculectomy



## Efficacy

Stronger IOP lowering agents Supporting to non responders

## Safety

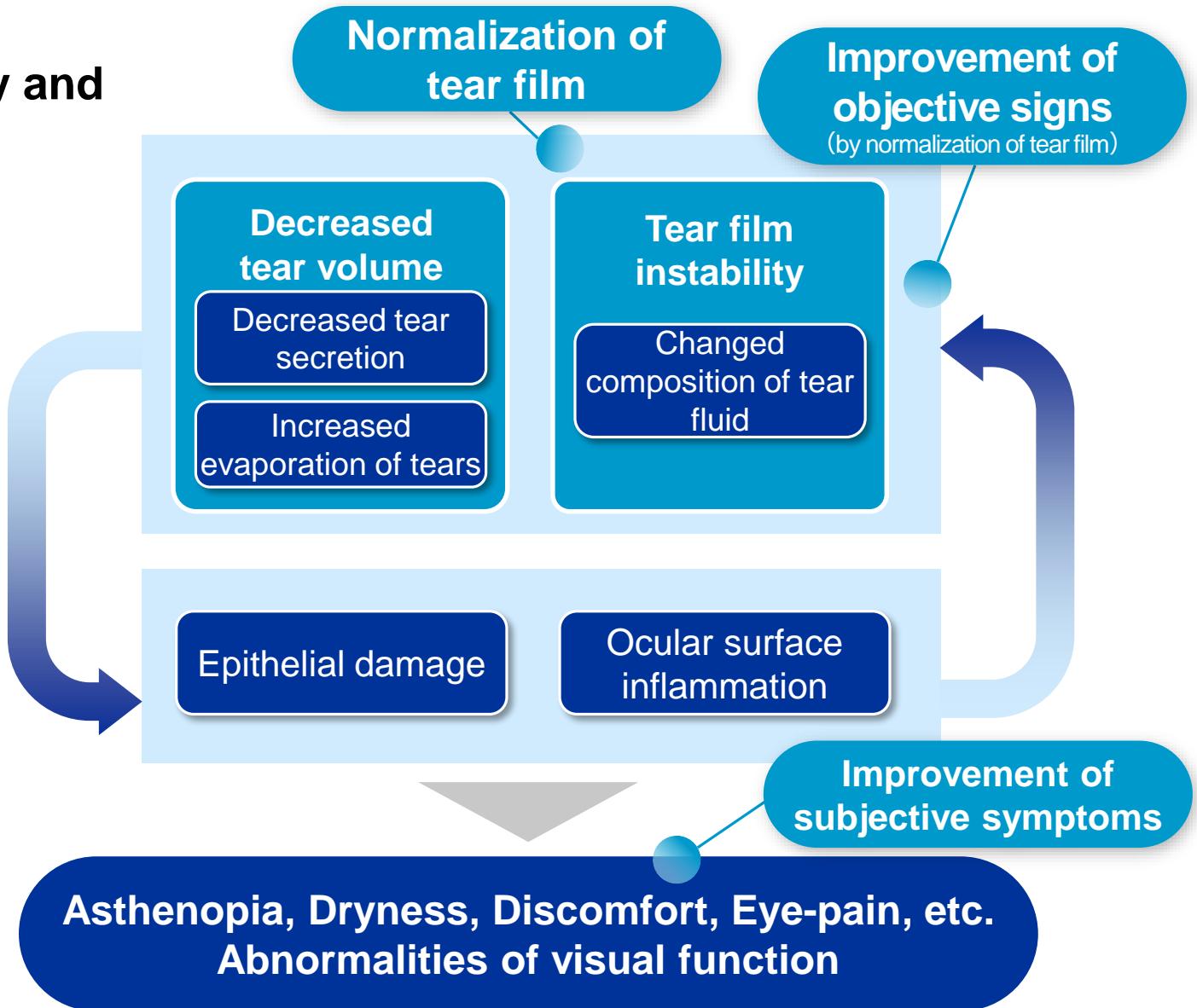
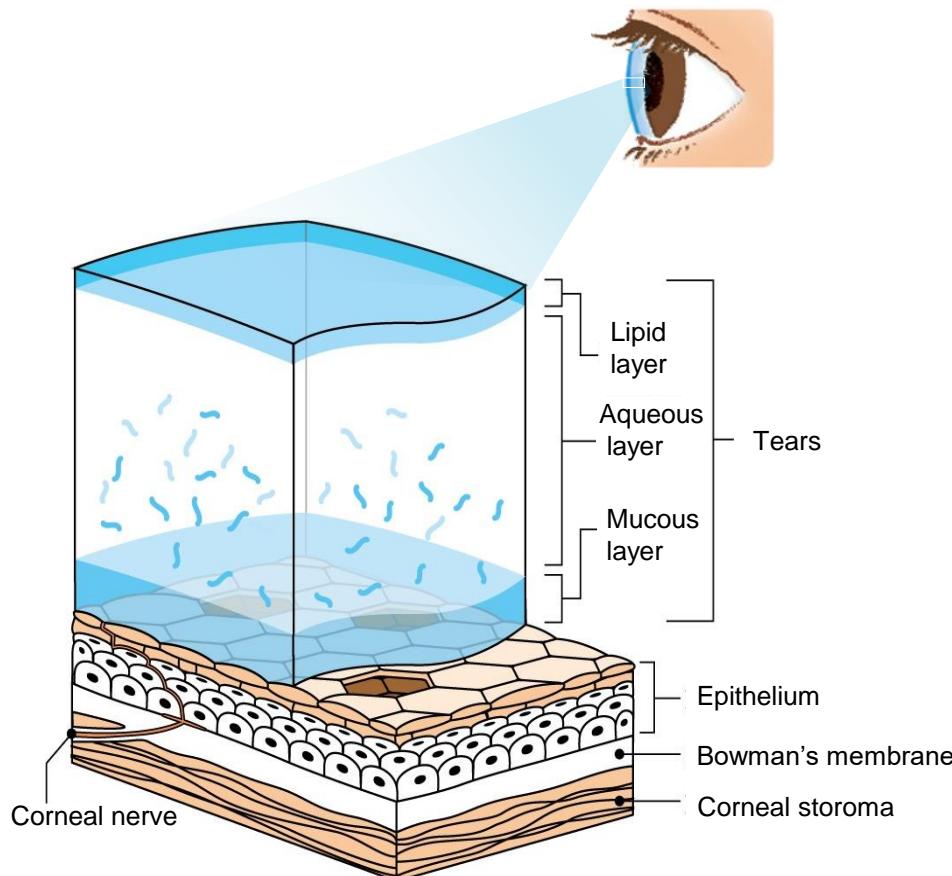
Reduction and avoidance of adverse reactions  
Reduction of invasiveness and complications of surgery

## Usability

Improve compliance  
Reduce Patients' burden (Easy to drop)

# Dry-eye: Improve Condition by Targeting Causative Mechanism

A disease that can decrease productivity and worsen the QOL over time.

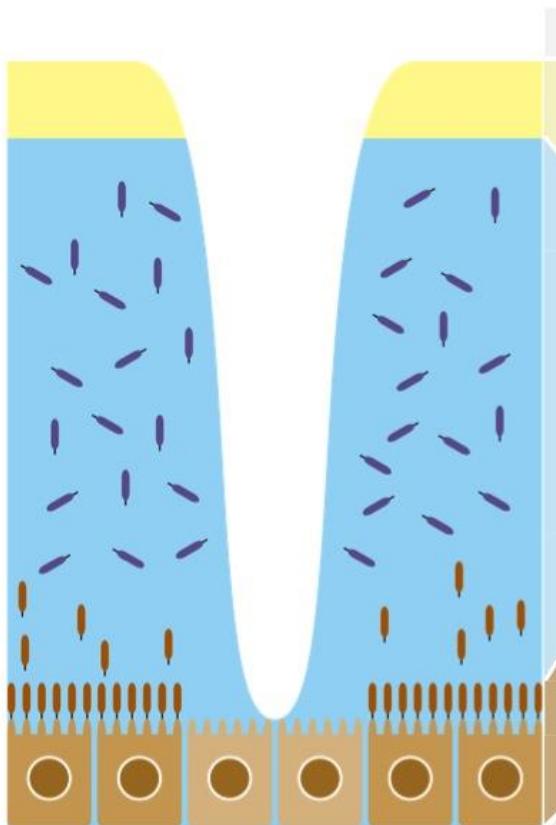


# Dry-eye: Product line for Tear Film Oriented therapy



## TFOT (Tear Film Oriented Therapy)

Ver.1



Target for Therapy		Topical eye therapy	
Lipid layer		Warm compress and lid hygiene Low-dose ophthalmic ointment Certain types of OTC <b>*Diquafosol sodium</b>	
Aqueous / Mucous layer	Aqueous component	Artificial tears Sodium hyaluronate <b>Diquafosol sodium</b> Punctal plug	
	Secretory mucin	<b>Diquafosol sodium</b> <b>Rebamipide</b>	
Epithelium	Membrane associated mucins	<b>Diquafosol sodium</b> <b>Rebamipide</b>	
	Epithelial cells (Goblet cell)	Autologous serum EGF (Rebamipide)	
Ocular surface inflammation		<b>Cyclosporin</b> <b>Steroids</b> <b>**Rebamipide</b>	

\*Diquafosol sodium may increase the function of the tear film lipid layer by promoting spreading of the lipid layer through lipid and tear fluid secretion.

\*\*Rebamipide may suppress the inflammation of the ocular surface in dry eye by its anti-inflammatory action.



Diquas  
3%



Hyalein  
0.1%



Soft Santear  
(OTC)



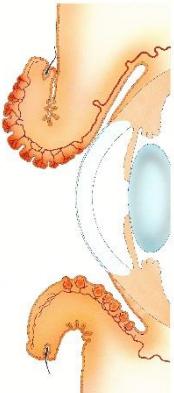
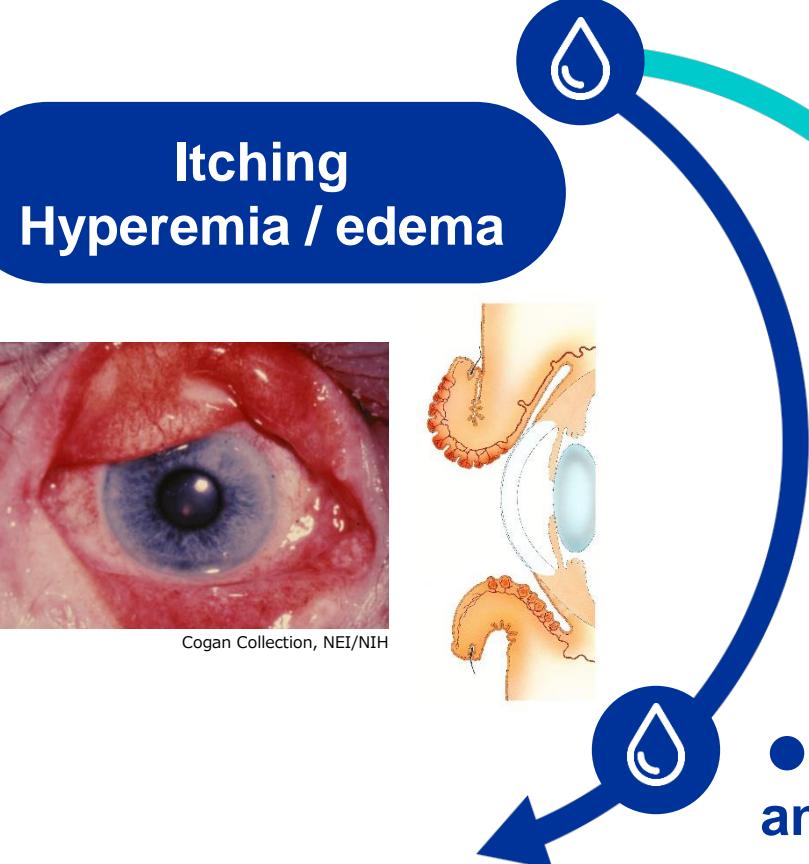
Cationorm® MD /  
Cationorm® SD



Ikervis®

Supervision: Dry Eye Society

# Allergic Conjunctivitis: Provide Treatment to All Patients from Mild to Severe



## ● Improvement of main symptoms

Anti-histamine ophthalmic solution  
Chemical mediator release inhibitors



Alegysal  
0.1%



Alesion  
0.05%



Lecrollyn® SD

## ● Improvement of safety and usability

BAK free  
Reduce dose frequency



Reduce dose frequency

4 times/day → 2 times/day

## ● Improvement of main symptoms

Anti-inflammatory ophthalmic solution



Flumetholon  
0.1%



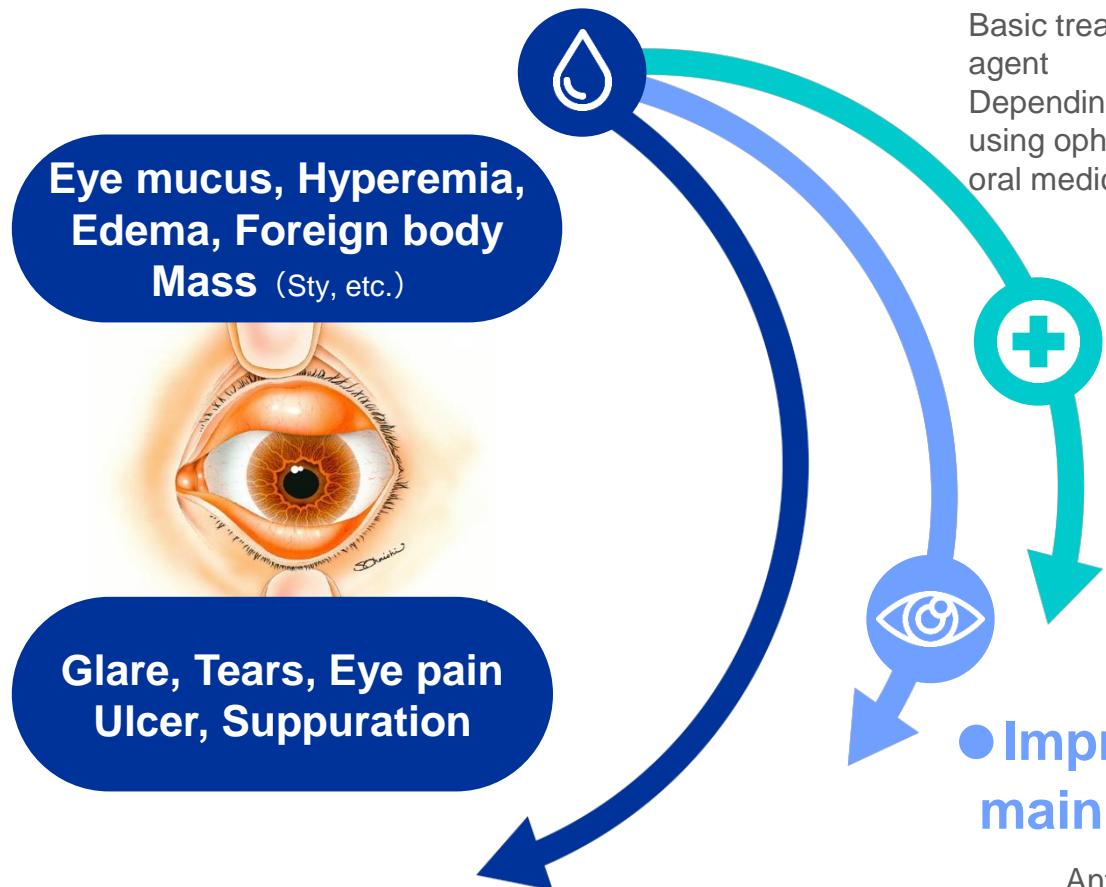
Verkazia®



Papilock Mini  
0.1%

\* For vernal conjunctivitis

# Ocular Infection: Introduce Wide Range of Product Line to Emerging Countries



## ● Antibacterial

Basic treatment with antibacterial agent  
Depending on the type of bacteria,  
using ophthalmic ointment and  
oral medicine



Tarivid  
0.3%



Cravit  
0.5%



Cravit  
1.5%



Ecolicin ophthalmic  
ointment



Tarivid  
ophthalmic ointment

## ● Antiviral

Antiviral ophthalmic solution  
Antiviral ophthalmic ointment



Zovirax  
ophthalmic ointment



Flumetholon  
0.1%



Proranon  
0.1%



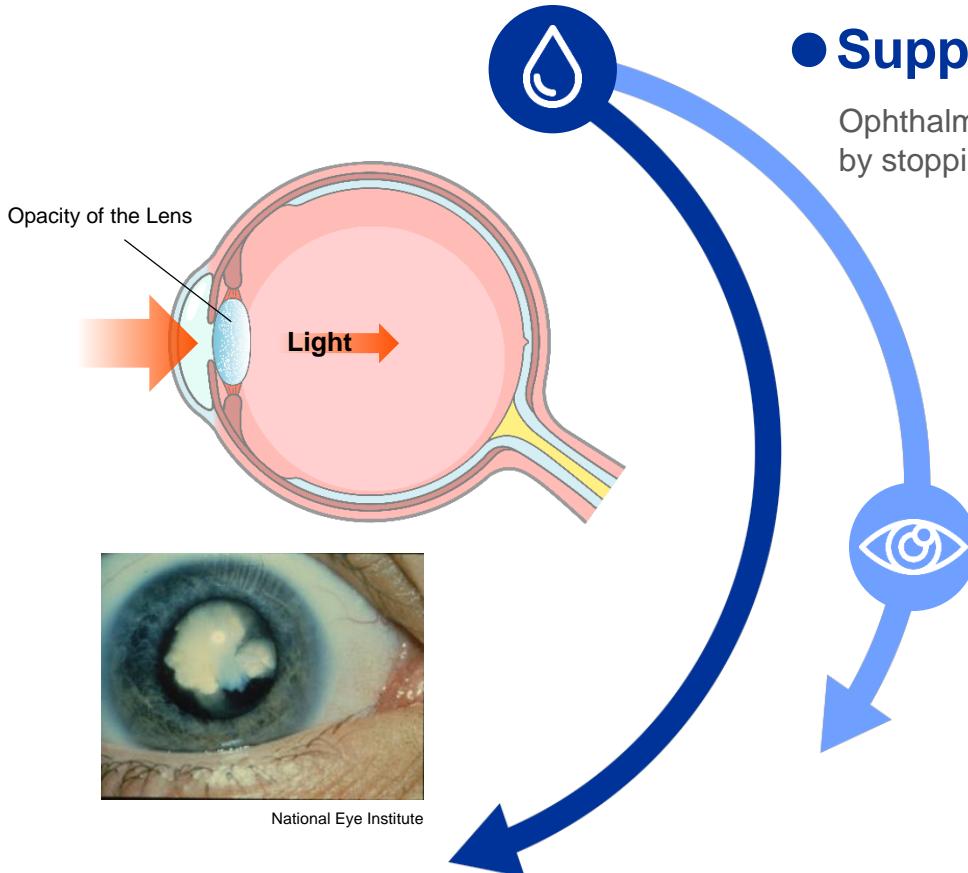
Santeson  
ophthalmic ointment

## ● Improvement of main symptoms

Anti-inflammatory  
ophthalmic solution

# Cataract: New Concept Intraocular Lens

51% cause of blindness in the world<sup>\*1</sup>. Affects all over 80 years old.<sup>\*2</sup>



## ● Suppression of lens opacity

Ophthalmic agent to suppress lens opacity by stopping degeneration of lens protein



Kary Uni  
0.005%

## ● Cataract surgery

The lens that has become cloudy is removed and replaced with an intraocular lens



Eternity



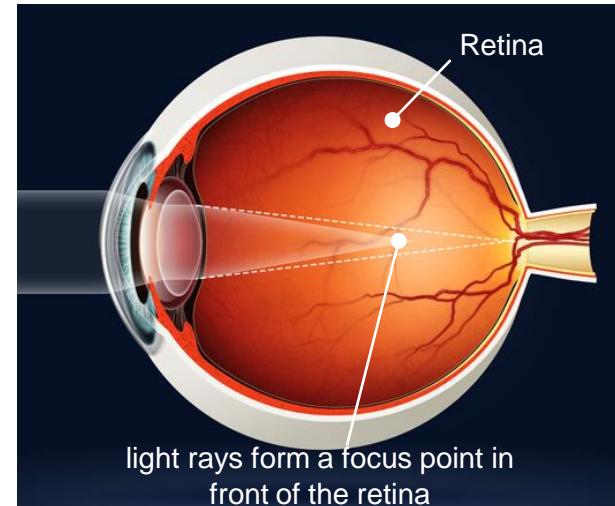
Lentis Comfort®

\*1: WHO Global Data on Visual Impairments 2010

\*2: 科学的根拠 (evidence) に基づく白内障診療ガイドラインの策定に関する研究 2002

# Myopia: Aim to Develop and Provide the World's First Treatment

27% of the world population is estimated to have myopia\*. Forecast to increase in the future.



## Suppression of the axial length elongation

Low dose atropine

## Vision Correction

Eye glasses, Contact lenses, LASIK

## Treatment of the cause of vision loss

Regression of neovascularization (Anti-VEGF therapy)

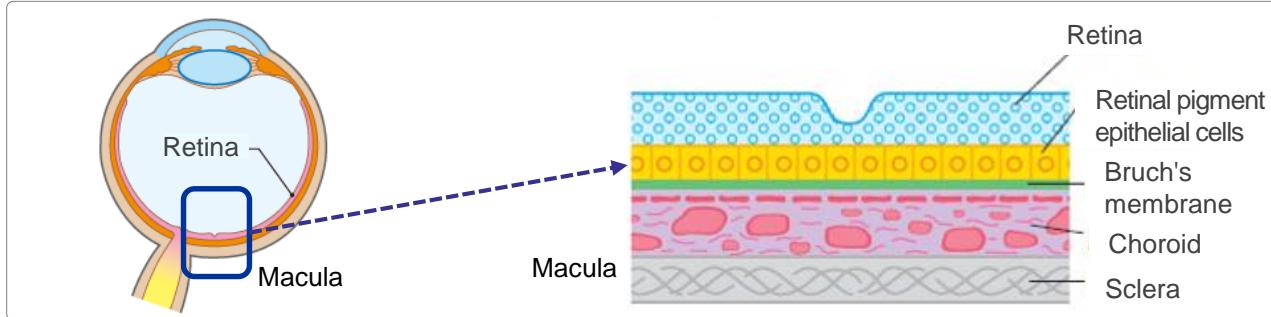
## Axial length growth

## Pathologic myopia

## Vision loss

\*: IMPACT OF INCREASING PREVALENCE OF MYOPIA, Report of the Joint World Health Organization

# Retina/Uveal Diseases: Aim to Provide Better Treatment Option



## wet Age-related Macular Degeneration (wetAMD)

Abnormal blood vessels begin to grow toward the macula. Then, the macula is impaired and can result in a severe loss of central vision.

## Diabetic Retinopathy (DR) Diabetic Macular Edema (DME)

The retina is damaged due to diabetes. If edema develops in macula (DME), it directly linked to vision loss.

## Central Retinal Vein Occlusion (CRVO) Branch Retinal Vein Occlusion (BRVO)

Retinal hemorrhage and edema caused by the retinal vein occlusion. If this extends to the macula, vision loss occurs rapidly.

## Posterior Uveitis

Inflammation occurs in the uvea (choroid) due to various causes, resulting blurred vision, ocular floater, photophobia and vision loss.

### Anti-VEGF therapy

Regression of the neovascular vessels and inhibition of neovascularization

### Anti-TNF $\alpha$ therapy

### Steroid

### Photodynamic therapy (PDT)

### Laser photocoagulation

Laser cauterize the lesion or related tissue.

### Steroid

### Anticoagulant (Oral)

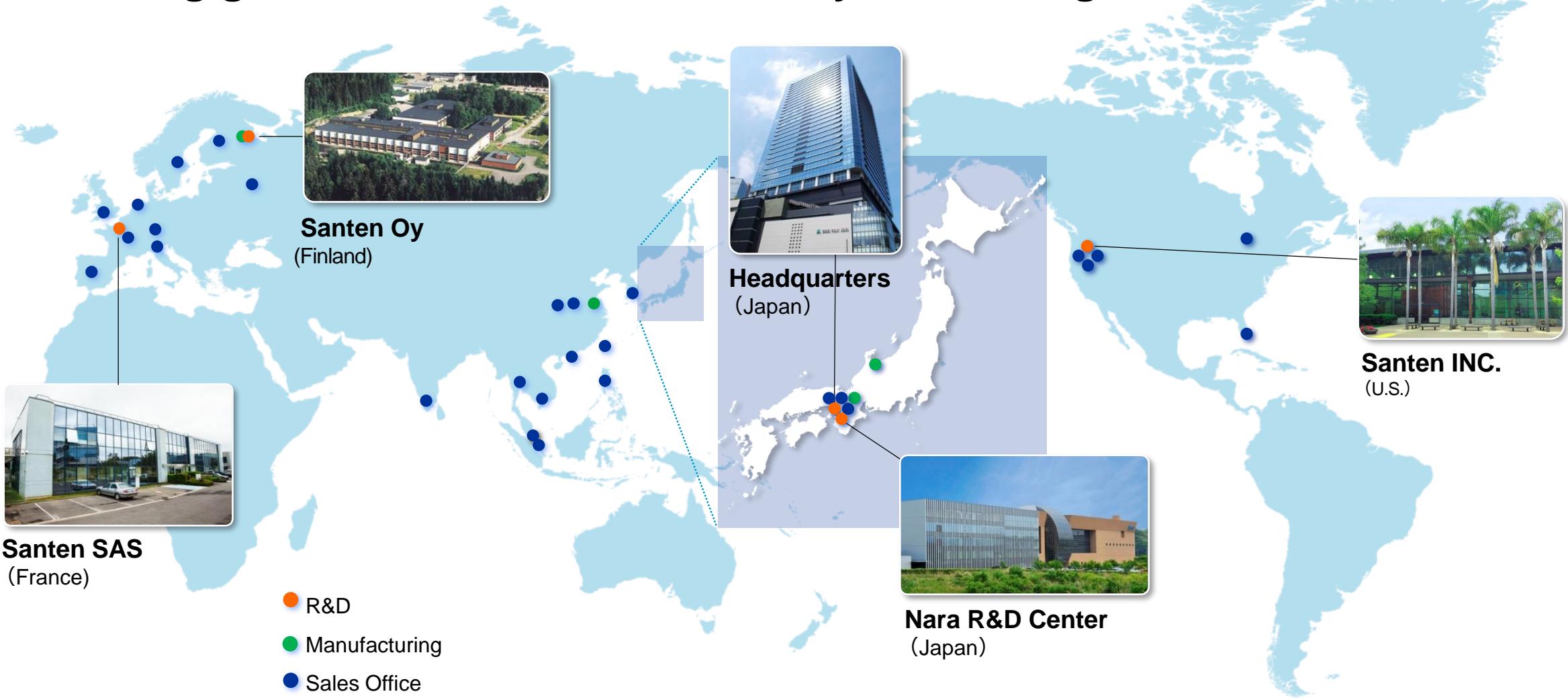
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# **Global R&D Network and Expedite Product Creation**

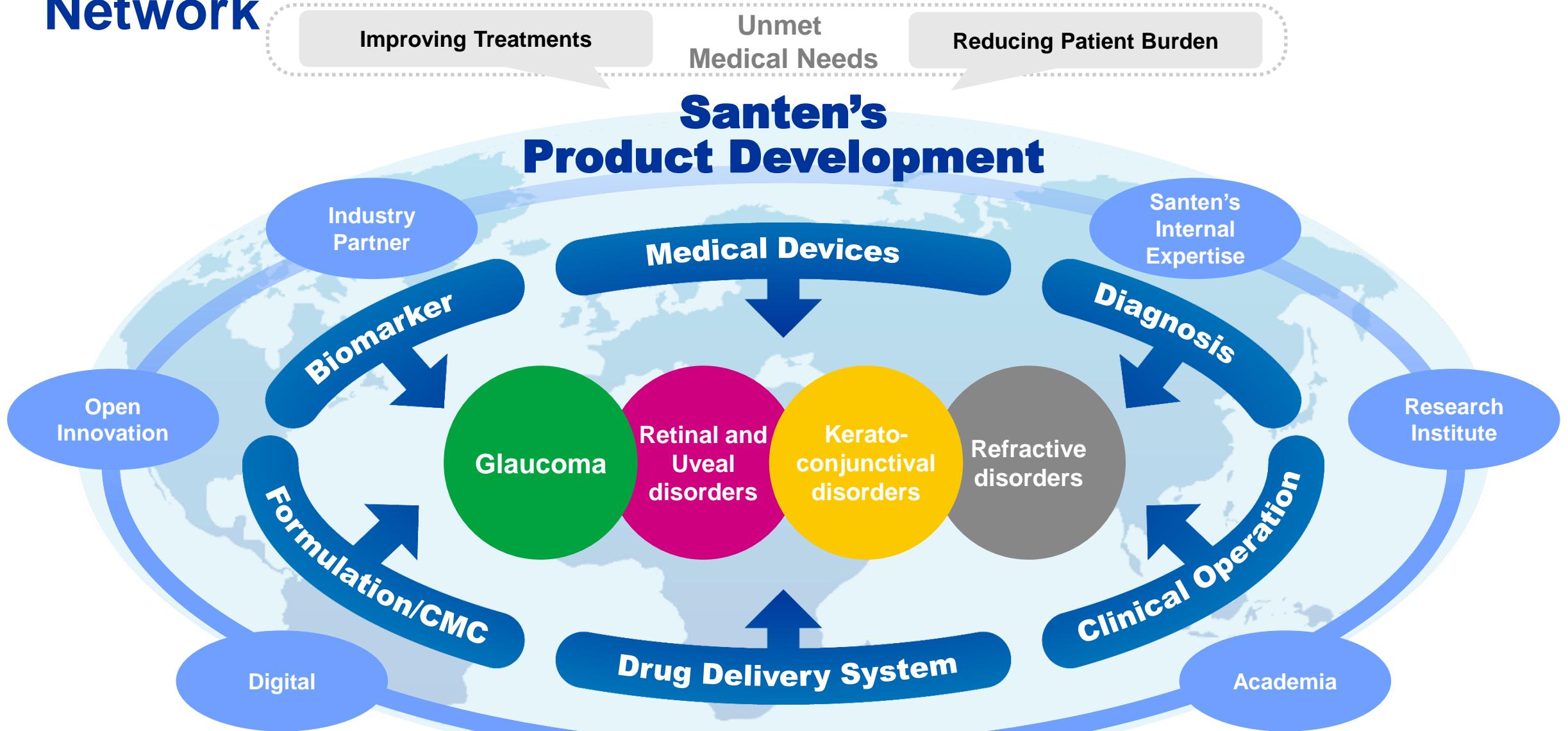
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# Santen's Global R&D Network

Addressing global unmet medical needs by networking around the world.



# Expedite Product Creation by Leveraging Global R&D Network





# Network Product Development

Expanding Partnerships globally



Academia



Research Institute



# Santen

Industry Partner



**AGC ASAHI GLASS**



Regenerative  
Patch Technologies™



**UBE UBE INDUSTRIES,LTD.**



**Oxford Biomedica**

# Improve PTS\*

## Building of Evidence for “Evidence Based Medicine” (Epidemiology)

Enhancement of clinical evaluation technology  
Banking of clinical samples

Clinical Research  
(Individual)

Translational research in the  
narrow sense

Validation of MOA in human  
Analysis of pathology

## Higher PTS & Productivity

Basic  
research

Clinical Research  
(Cohort)

Clinical epidemiology,  
Pharmacoepidemiology,  
Proteomics, Genomics

Clinical data analysis  
Analysis of biospecimen

\*Probability of Technical Success

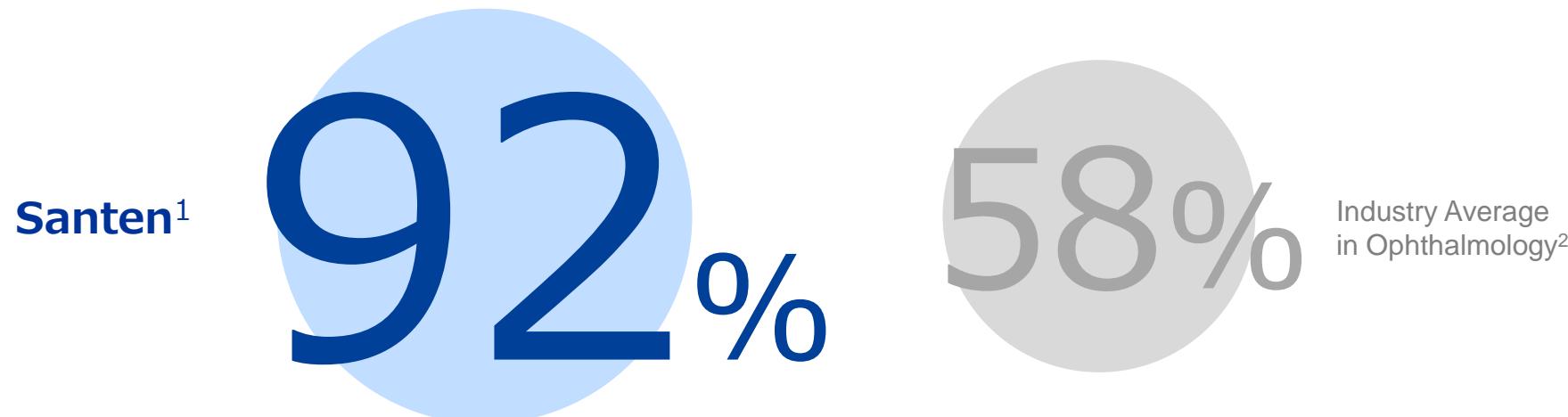
# Clinical Development that are Fast and Have Higher Success Rates



- Speed of clinical trials DE-117 clinical trials (Glaucoma)



- Phase 3 success rates in ophthalmology



1. Internal analysis in 2006-2018

2. Clinical Development Success Rates 2006-2015, Bio, Biomedtracker, Amplion, 2016

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# Pharmaceutical Development

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# Innovative Pharmaceutical Development to Meet Customer Needs



## Less frequency

Reduce frequency of instillation  
Reduce complexity by using many of combination



## Improve usability

Continuous treatment by improving adherence and compliance

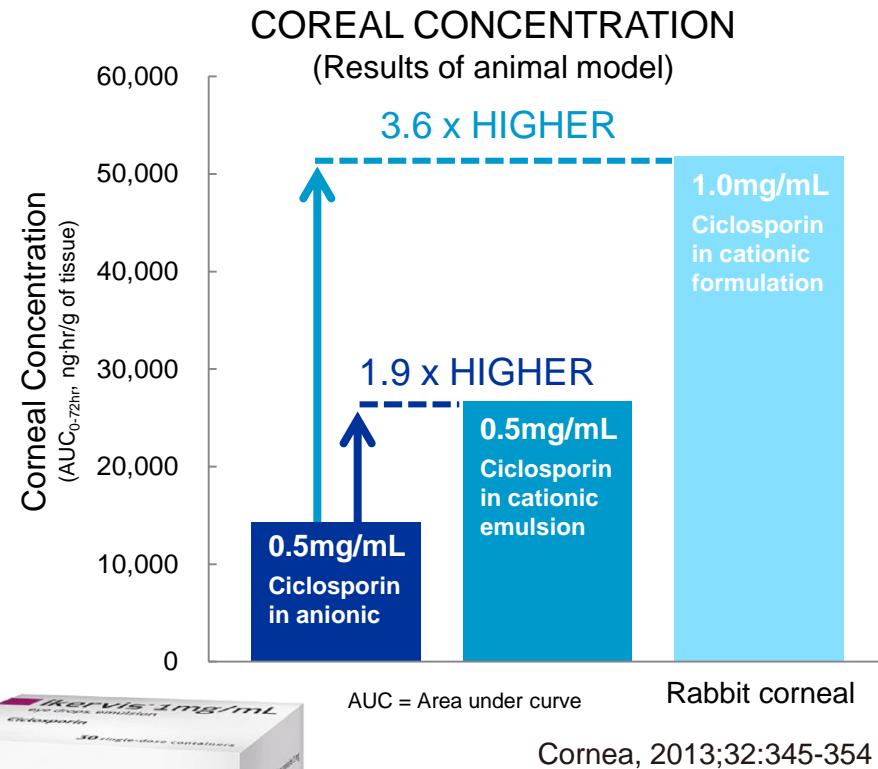
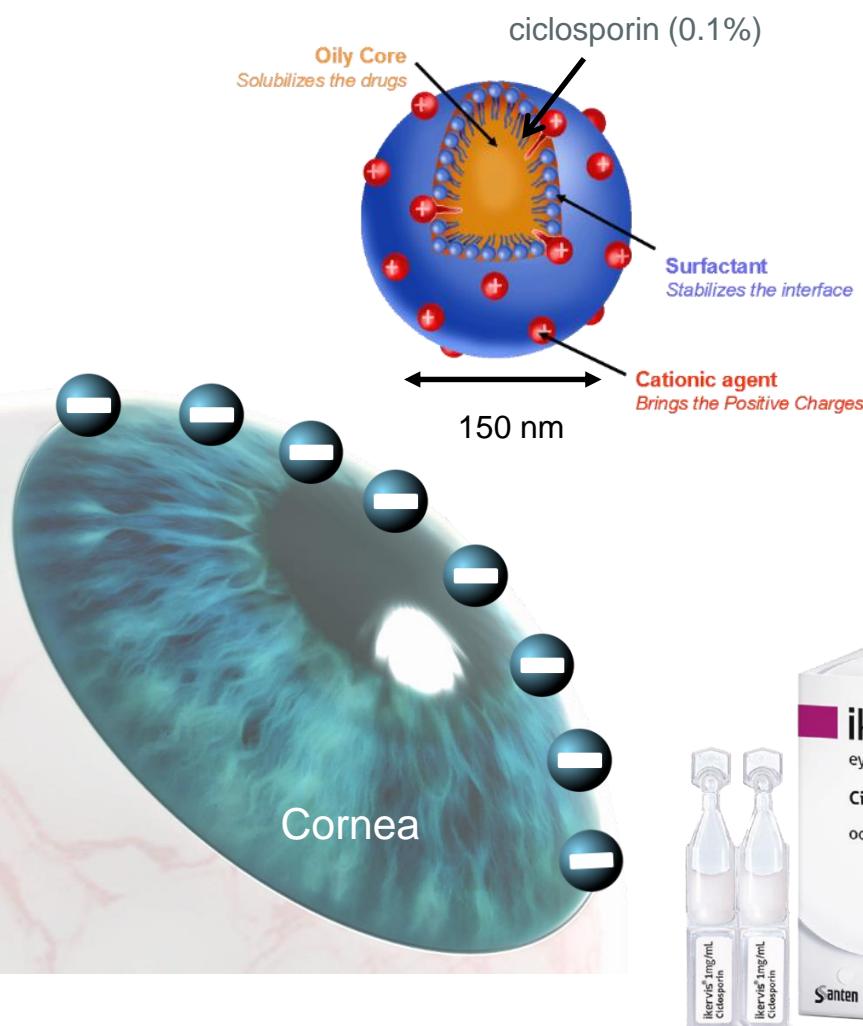
## Ophthalmic Solution with High Safety

Reduce the effect on ocular surface by preservatives.

## Easy-to-use bottle

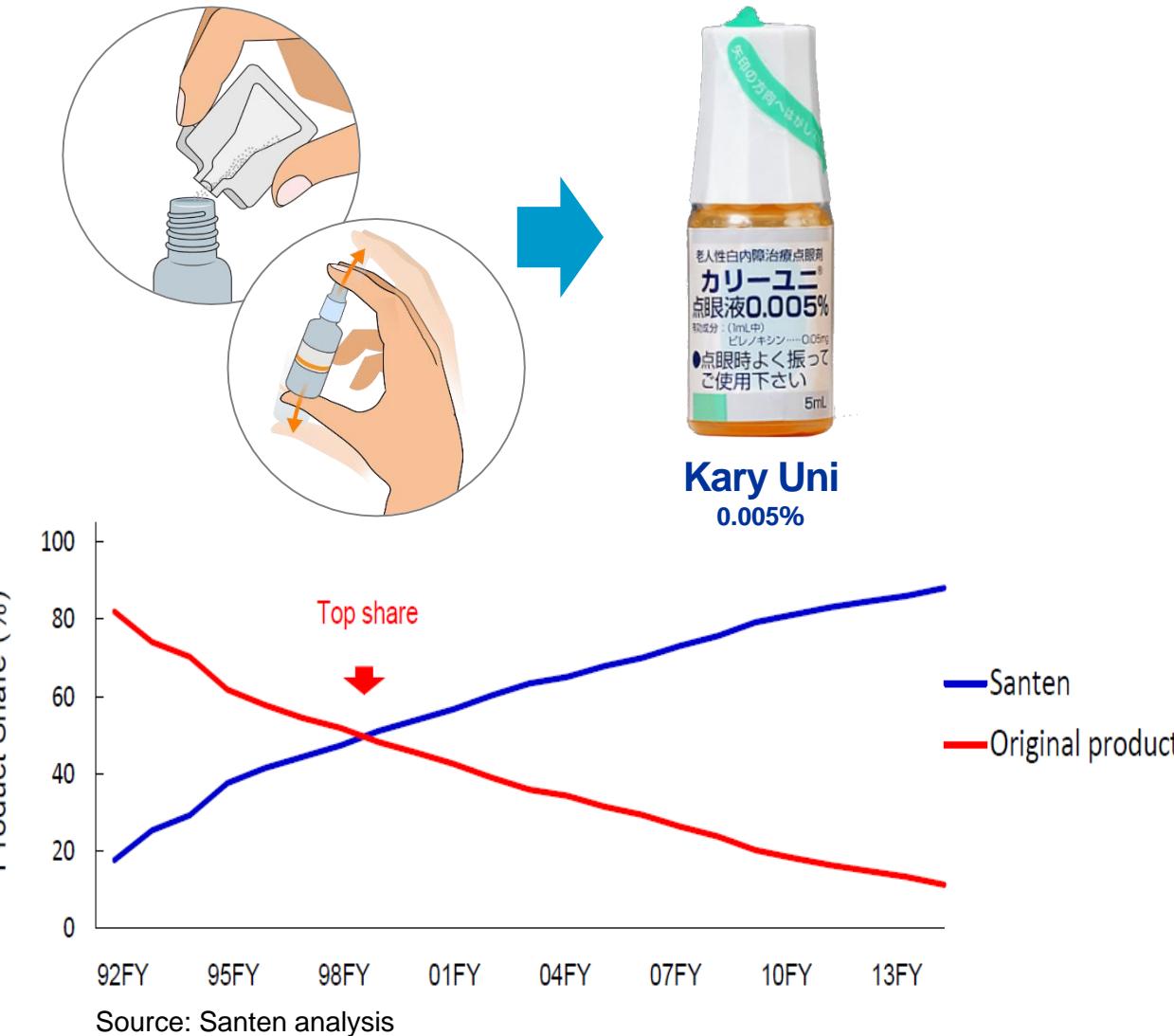
Develop easy-to-use bottle for everyone including elderly

# Less frequency: Reduce Patient Burden



Tapcom

# Improve usability: Support Patients' Adherence to Treatment



# Ophthalmic Solution with High Safety: Prevent Treatment Withdrawal



Low BAK

Conventional preservative



Benzalkonium Chloride

Low Preservative in new formulation

Benzalkonium Chloride  
(Low Concentration)

BAK Free

Other Preservative in new formulation

Chlorhexidine gluconate solution



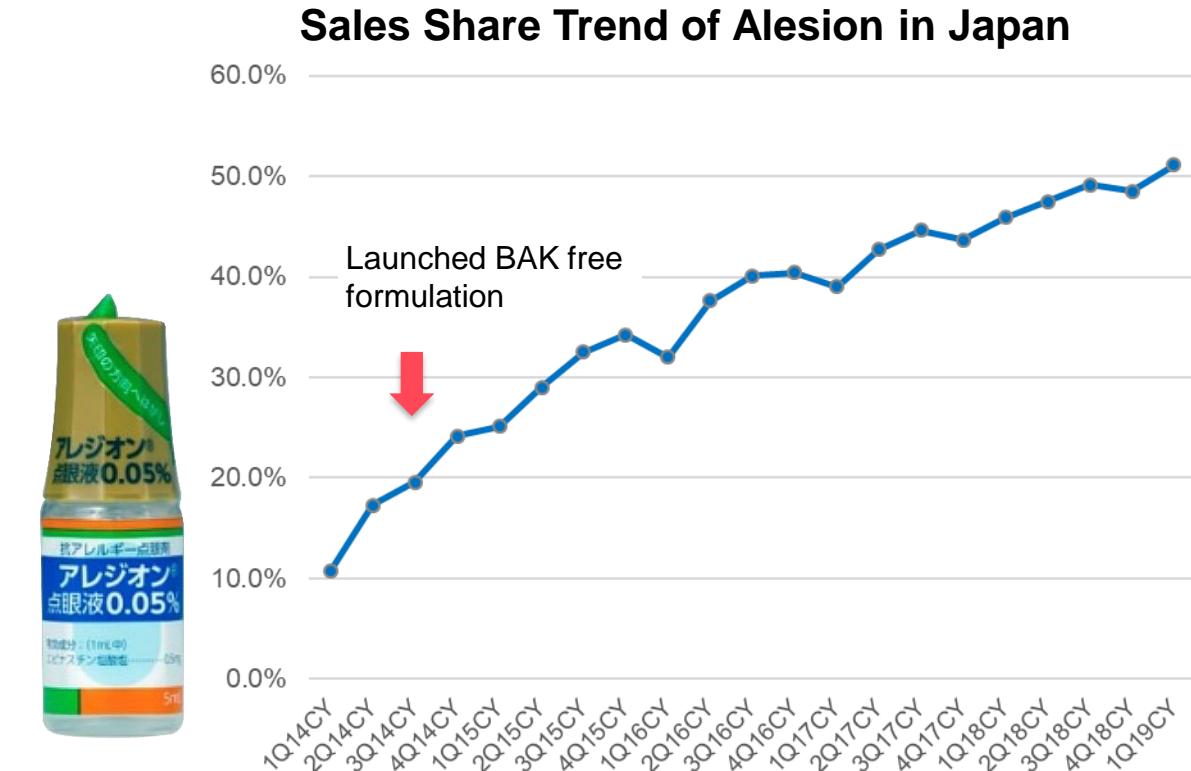
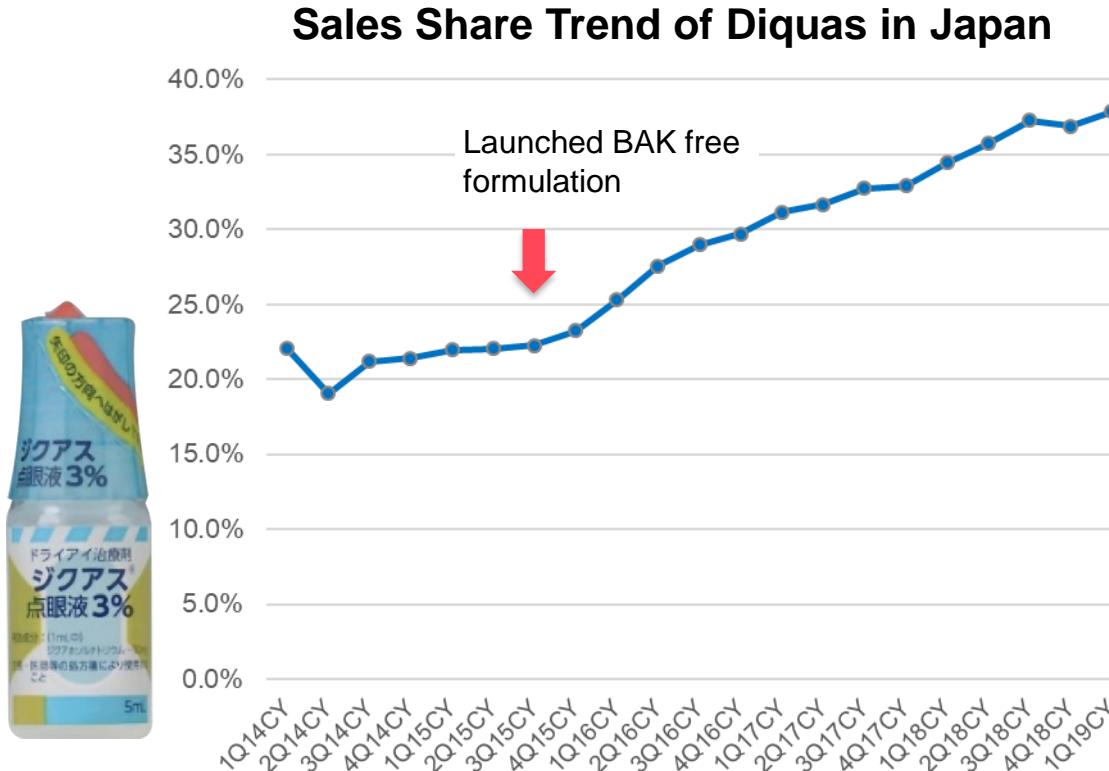
Preservative Free

Preservative Free in new formulation

N/A

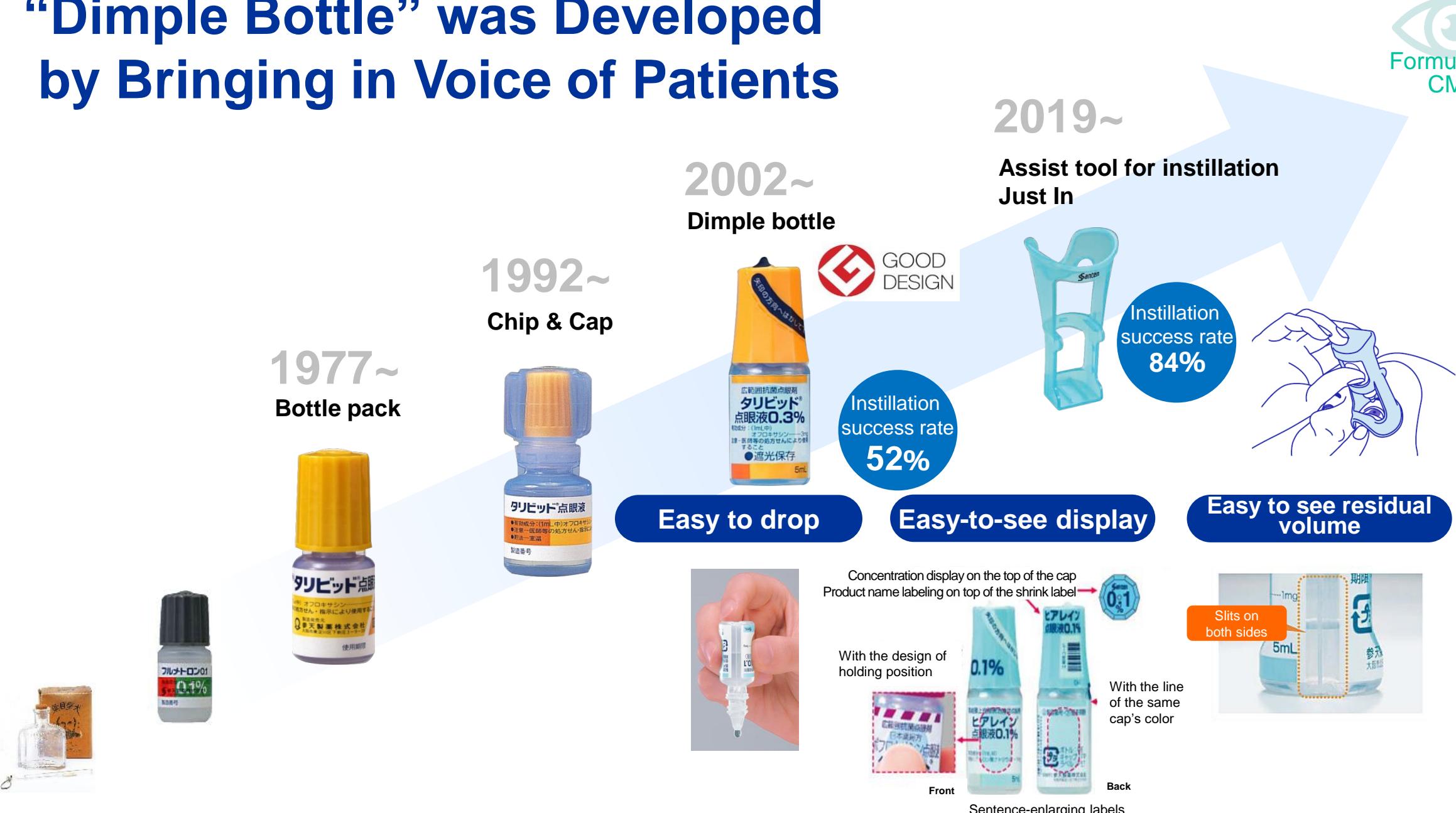


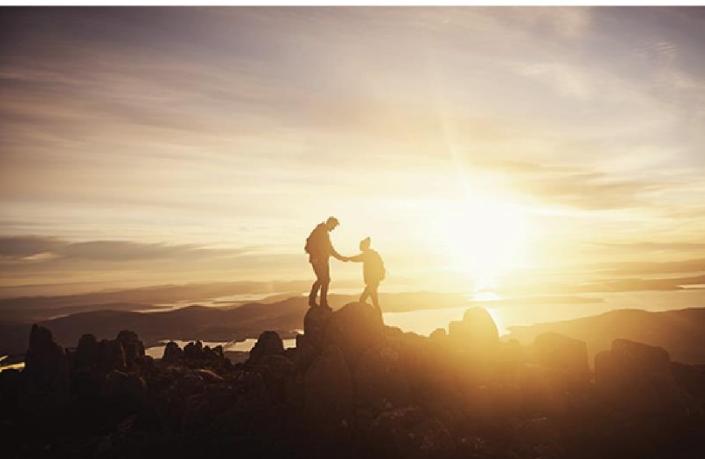
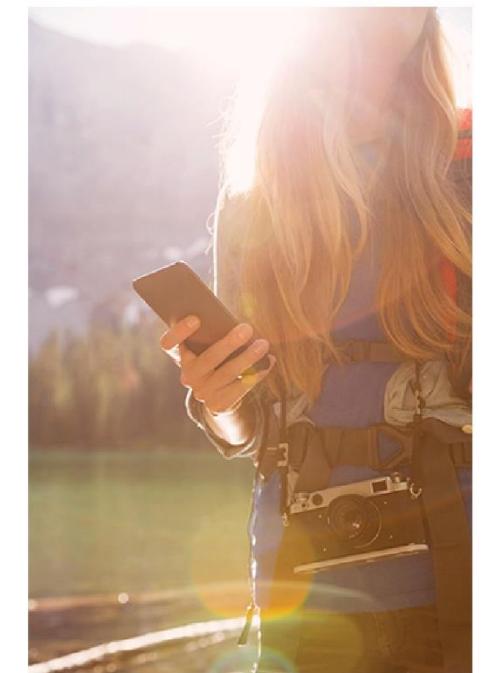
# Ophthalmic Solution with High Safety: Promote Continuous Business Grow



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# “Dimple Bottle” was Developed by Bringing in Voice of Patients





**VISION  
EVERY  
DAY.**

SANTEN R&D:  
**VANGUARDS OF VISION**



**Santen**

# R&D Leadership Members



**Reza Haque**

Senior Vice President,  
Head of Biomedical  
Strategy & Research



**Naveed Shams**

Senior Corporate  
Officer & CSO,  
Head of R&D Division



**Kenji Morishima**

Corporate Officer,  
Head of Pharmaceuticals &  
Pharmacology  
Representative, Asia R&D



**Peter Sallstig**

Senior Vice President,  
Head of Product  
Development



**Takeshi Matsugi**

Head of R&D Strategic  
Operations

